

Solvent-free bentonite-catalyzed condensation of malonic acid and aromatic aldehydes under microwave irradiation

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Solvent-free condensation between malonic acid and aromatic aldehydes is studied in the presence of bentonite. Various diacids are prepared in good to moderate yields and in very short reaction times under microwave irradiation.

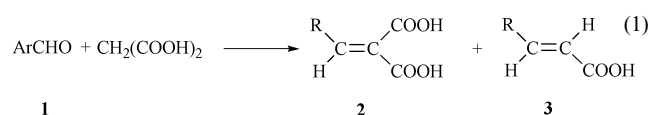
Introduction

Recently, microwave-assisted solvent-free synthesis¹ in organic reactions has been of growing interest as an efficient, economic and clean procedure ('green chemistry').² Over the past few years, a considerable number of reactions have been developed in which inorganic solid supports such as aluminas, silica gels and montmorillonites appeared to be useful in terms of mildness of conditions, yield and convenience.³ We have shown earlier that diethyl malonate, ethyl cyanoacetate, malonic acid and several different types of aldehyde could be efficiently condensed in chlorobenzene or in 'dry media' in the presence of basic alumina.⁴⁻⁶ In the present communication, we report our results on this environmentally benign approach for the bentonite-catalyzed condensation between malonic acid and various aromatic aldehydes such as benzaldehyde, *o*- or *p*-tolualdehyde, 2-chlorobenzaldehyde, *p*-anisaldehyde, 1-naphthaldehyde and 2-furaldehyde under microwave irradiation in 'dry media'.

Results and discussion

We first examined the relative concentration effects between *p*-tolualdehyde **1c** and malonic acid under microwave conditions [eqn. (1)] (Table 1).

The main products under these conditions were the diacids **2**.



Ar: **a**=C₆H₅; **b**=*o*-CH₃-C₆H₄; **c**=*p*-CH₃-C₆H₄; **d**=*p*-OCH₃-C₆H₄
e=*o*-Cl-C₆H₄; **f**= α -naphthyl; **g**=2-furyl

The best results (in italics) were obtained with the mixture of composition **1c**: malonic acid = 1 : 3 w/w for an irradiation time of 5 min in the presence of bentonite (entry 4, 86%). Irradiation time also significantly affected the yields. Thus, increasing the reaction time up to 5 min enhanced the yield (entries 4, 5 and 6). However we could not improve the yield even after prolonged irradiation (9–15 min, entries 7 and 8). In the absence of bentonite, the formation of product was very low (entry 9).

After we had optimized the reaction conditions, we investigated the effect of the amount of bentonite on the reaction of *p*-tolualdehyde **1c** and malonic acid under microwave irradiation (Table 2).

Table 2 shows that the yields were highly dependent on the quantity of support. In the absence of bentonite, only traces of product were detected (entry 1). Maximum yield was obtained when the mass ratio of bentonite and malonic acid was 1.4 : 1 (entry 4). However, isolated yields were decreased when using larger amounts of support (entries 5, 6).

Table 1 Effect of the relative amounts of *p*-tolualdehyde **1c** and malonic acid under microwave irradiation in the presence of bentonite (bentonite : malonic acid = 1.38 : 1)

Entry	<i>p</i> -Tolualdehyde		Malonic acid		Time (<i>t</i> /min)	Yield ^a 2c (%)
	g (mmol)	Equiv.	g (mmol)	Equiv.		
1	0.20 (1.67)	1.5	0.12 (0.11)	1	5	15
2	0.20 (1.67)	1	0.26 (2.51)	1.5	5	32
3	0.20 (1.67)	3	0.06 (0.56)	1	5	9
4	<i>0.20 (1.67)</i>	<i>1</i>	<i>0.52 (5.01)</i>	<i>3</i>	5	86
5	0.20 (1.67)	1	0.52 (5.01)	3	1	28
6	0.20 (1.67)	1	0.52 (5.01)	3	3	37
7	0.20 (1.67)	1	0.52 (5.01)	3	9	74
8	0.20 (1.67)	1	0.52 (5.01)	3	15	65
9	0.20 (1.67)	1	0.52 (5.01)	3	5 (neat)	3 ^b

^a Yield of isolated product based on *p*-tolualdehyde. ^b No bentonite was used.

Table 2 Effect of the amount of bentonite on the reaction of *p*-tolualdehyde **1c** (0.20 g) and malonic acid (3 equiv., 0.52 g) under microwave irradiation (5 min)

Entry	Bentonite/g	Yield ^a 2c (%)
1	0	3
2	0.24	55
3	0.36	80
4	0.73	86
5	1.45	73
6	2.18	52

^a Yield of isolated product based on *p*-tolualdehyde.

Table 3 Comparison between classical heating and microwave irradiation (MW) in the absence or presence of bentonite at 80 °C for the reaction of benzaldehyde **1a** (1.8 mmol, 0.20 g) and malonic acid (3 equiv., 5.4 mmol, 0.56 g)

Entry	Bentonite/g	Heating time (<i>t</i> /min)		
		MW	Classical heating ^a	Yield ^b 2a (%)
1	0		5	0
2	0	5		Trace
3	0.80		5	9
4	0.80		900	74
5	0.80	5		79

^a Oil-bath with reflux condenser (bath temperature = 80 °C). ^b Yield of isolated product based on benzaldehyde.

In order to check the possible intervention of specific (not purely thermal) microwave effects, the reaction was performed in one case under similar experimental conditions (weight of reactants, time and temperature) using a thermostatted oil-bath (conventional heating). The temperature was measured in the reaction medium using a thermometer either under microwave irradiation (at the end of the reaction) or under classical heating (Table 3).

For comparison, the mixtures were heated (80 °C) to the temperature attained by the bentonite just after microwave irradiation for 5 min (78–80 °C). As shown in Table 3, we could not isolate a product in the absence of bentonite (entries 1 and 2). Under the same conditions with bentonite the thermal activation (80 °C) did not give good yields (entry 3). Microwave irradiation allowed a drastic reduction of reaction time as comparable yields were obtained using 5 min of irradiation in a domestic microwave oven (entry 5), while under classical heating the reaction time required 900 min of stirring at 80 °C even with lower yields (entry 4).

It is evident that very strong specific effects of microwaves were operating here to induce enhancements yet to be seen in a lot of cases in organic synthesis.^{1,7}

In order to extend the scope of this method, the condensations of aromatic aldehydes with malonic acid in the presence of bentonite were successfully performed. The results are summarized in Table 4.

It was finally interesting to compare the support influence according to their acidity. We carried out the reaction using other solid supports such as silica gel, K10 and KSF (Table 5).

In all cases, diacids **2** were obtained as the major product and (*E*)-cinnamic acids **3** were detected as minor products in ¹H NMR spectra. Clays K10 and bentonite have been shown to be good supports in terms of yields. The selectivity obtained with K10 was superior to that with bentonite despite the disadvantages of stronger acidity and higher cost. The product ratio of diacid **2** and monoacid **3** is shown in Table 5.

In order to try to understand the differences in behaviour between these solid supports, we indicate in Table 6 some important characteristics of these supports upon considering

Table 4 Bentonite-catalyzed condensation between various aldehydes and malonic acid (amounts of products) under microwave irradiation for 5 minutes

Aldehyde	Product	Mp (θ/°C)		Yield 2 (%)
		Found	Lit. [ref.]	
1a	2a	193–195	194–196 [8]	79
1b	2b	195–196	193–194 [6]	82
1c	2c	205–208	207–210 [9]	86
1d	2d	184–187	185–188 [8]	88
1e	2e	194 (decomp.)	196 [10]	94
1f	2f	198–200	199–203 [11]	94
1g	2g	196 (decomp.)	197 (decomp.) [12]	75

Table 5 Microwave-irradiated condensation between benzaldehyde **1a** and malonic acid using various solid supports

Solid support	Ratio ^a	
	2a ^b	3a
Bentonite	92 (79)	8
Silica gel	95 (74)	5
K10	98 (80)	2
KSF	88 (63)	12

^a Ratios were determined by ¹H integration using 300 MHz NMR spectroscopy. ^b In parentheses, yield of isolated product based on benzaldehyde.

Table 6 Some characteristics of the supports¹³

Solid support	<i>H</i> _o Hammett acidity	Surface area/m ² g ⁻¹
Bentonite	+1.5 to -3.0	500–700
Silica gel	+6.8 to +4.0	500–600
K10	-5 to -6	220–270
KSF	-8	20–40

two main properties: their acidity as evaluated in the solid state by *H*_o Hammett functions and their capacity in absorbing organic molecules as connected to their specific areas.

Acidity seems not to be the only important factor. In fact, K10 and bentonite lead to closely related results, which are very different from those with KSF, a clay with rather similar acidity (Table 6). It seems evident that some other factors, certainly such as surface area, may play a decisive role in the reaction. The supports with higher surface areas lead to the best results. They are indicative that the reaction occurs mainly when the reactions are effectively absorbed on the support, a fact which is confirmed by the effect of the amount of bentonite (Table 2).

Conclusions

In summary, we have demonstrated the bentonite-catalyzed condensation between malonic acid and various aldehydes under irradiation in a domestic microwave oven. This method offers some advantages in terms of simplicity of performance, non-aqueous work-up, no side products and low cost. In addition, the bentonite can be recycled after activation (yields remained 79% after 3 re-uses) in the reaction of benzaldehyde **1a** and malonic acid.

We have also to underline that under our conditions diacids were selectively obtained, whereas cinnamic acids (monoacids) were obtained in a basic medium (piperidine in pyridine,¹⁴ ethanol¹⁵ or ammonium acetate under solvent-free conditions¹⁶) under MW irradiation. The two methods appeared to be complementary. One has finally to quote the large discrepancy with the recent result published by Sampath Kumar *et al.*¹⁷ who obtained the (*E*)-cinnamic acids under MW (emitted

power = 600 W within 4 min) in the presence of silica gel (activated at 140 °C for 3 hours prior to use). Maybe a different quality of support or, more certainly, higher temperature levels were involved in their experiments.

Experimental

Mps were taken on a Haake Buchler mp apparatus and are uncorrected. Infrared spectra were recorded with an infrared spectrophotometer model Magna-IR 500 and are reported in wavenumbers. NMR spectra were determined in a d-chloroform/DMSO- d_6 solution mixture on an FT-NMR Bruker 300 (300 MHz) spectrometer and are reported in ppm using tetramethylsilane as the internal standard. Bentonite, montmorillonite K10, KSF (Aldrich Co.) and silica gel 60 (Merck, 70–230 mesh ASTM) were activated at 140 °C for 3 h prior to use. The reactions were carried out in a 2450 MHz commercial microwave oven (Sam Sung, Model # RE-555 TCW).

A typical procedure for the condensation of malonic acid and *p*-tolualdehyde **1c**

In a screw-capped vial were placed malonic acid (0.52 g, 5.0 mmol, 3 equiv.), *p*-tolualdehyde **1c** (0.20 g, 1.67 mmol) and bentonite (0.72 g). The tube was capped and the contents of the tube were thoroughly mixed with a vortex mixer and then irradiated in the microwave oven for 5 min at a power of 1050 W. After the reaction the mixture was cooled to room temperature and washed successively with hexane (3×10 mL) and cold water (3×10 mL). The resulting mixture was immersed in ethyl acetate (2×10 mL) for 5 min. After removal of bentonite by filtration under vacuum, the mixture was evaporated under reduced pressure to give 2-(4-methylbenzylidene)malonic acid **2c** as a white solid (0.29 g, 86%). This solid was recrystallized from hot, distilled water, mp 205–208 °C (lit.,⁹ 207–210 °C); ^1H NMR δ 7.43 (1H, s, vinyl H), 7.39 (2H, d, J 8.07 Hz), 7.06 (2H, d, J 8.07 Hz) and 2.32 (3H, s, Ar- CH_3); ^{13}C NMR δ_{C} 169.05, 166.20, 141.10, 139.59, 130.82, 130.11, 130.03, 127.90, 21.89; IR (KBr) ν_{max} 3320–2460 (COOH), 1701 (C=O), 1610, 1450, 1298, 1245 cm^{-1} .

All other products were identified by comparison with authentic samples (mp, TLC) and by their ^1H NMR and IR spectra.

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